

AMENDMENTS TO THE CLAIMS

1. (Withdrawn) An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide selected from the group consisting of the lectin domain of a mammalian polypeptide GalNAc-transferase, and a lectin-functional variant or fragment of said lectin domain, wherein said polypeptide does not encompass the intact, functioning catalytic domain of the enzyme.

2. (Withdrawn) A nucleic acid molecule according to claim 1 comprising a nucleic acid sequence selected from the group consisting of the nucleic acid sequences encoding the GalNAc-T1 to -T16 lectin domains set forth in Table III herein and lectin-functional variants and fragments thereof.

3. (Withdrawn) The nucleic acid of claim 2 further comprising 30-60 nucleotides of the corresponding GalNAc-transferase sequence at its 5' or 3' end.

4. (Withdrawn) The nucleic acid of claim 1 wherein the polypeptide GalNAc-transferase or lectin-functional variant or fragment of said lectin domain is human.

5. (Currently amended) An isolated lectin polypeptide consisting of a truncated mammalian GalNAc-transferase polypeptide comprising a domain selected from the group consisting of ~~comprising~~ the lectin domain of a mammalian polypeptide GalNAc-transferase, ~~or~~ a lectin-functional variant and fragments or fragment thereof, wherein:

(i) the lectin domain has lectin binding activity; and

(ii) the truncated polypeptide does not encompass the intact, functioning catalytic domain of the enzyme.

6. (Original) A lectin polypeptide according to claim 5 having an amino acid sequence selected from the group consisting of the amino acid sequences of GalNAc-T1 to -T16 set forth in Table III herein and lectin-functional variants and fragments thereof.

7. (Currently amended) The polypeptide of claim 6 further comprising 10-20 amino acid residues of the ~~the~~ corresponding GalNAc-transferase sequence at its carboxy or amino terminus.

8. (Original) The polypeptide of claim 5 wherein the polypeptide GalNAc-transferase or a lectin-functional variant or fragment thereof is human.

9. (Withdrawn) A method of producing a lectin polypeptide comprising the lectin domain of a mammalian polypeptide GalNAc-transferase or a lectin-functional variant or fragment thereof, said polypeptide not encompassing the intact, functional catalytic domain of said transfearse, the method comprising:

- (i) growing a host cell transfected with a nucleic acid sequence encoding the lectin domain of a mammalian polypeptide GalNAc-transferase or a lectin-functional variant or fragment of said lectin domain and excluding the intact catalytic domain of the enzyme under conditions suitable for lectin expression; and
- (ii) isolating the lectin polypeptide produced by the host cell

10. (Withdrawn) A method according to claim 9 wherein said nucleic acid sequence is selected from the group consisting of the sequences encoding the GalNAc-T1 to -T16 lectin domains stated in Table III herein and lectin-functional variants and fragments thereof.

11. (Withdrawn) The method of claim 9 wherein the polypeptide GalNAc-transferase or lectin-functional variant or fragment of said lectin domain is human.

12. (Withdrawn) A method of identifying a substance that binds to a polypeptide GalNAc-transferase lectin domain, which comprises

- (i) reacting a lectin polypeptide according to claim 5 with at least one substance which potentially may bind to the polypeptide, under conditions which permit the association between the substance and the polypeptide;
- (ii) removing and/or detecting the polypeptide with associated substance which, if present, indicates that the substance binds to the polypeptide.

13. (Withdrawn) A method of screening for inhibitors of functions mediated by polypeptide GalNAc-transferase lectin domains which comprises using a lectin polypeptide according to claim 5 in a binding assay where it interacts with a GalNAc or Gal β 1-3GalNAc O-glycopeptide ligand or a molecular mimic hereof, and measuring the binding inhibition to identify and evaluate efficiency of a potential inhibitor.

14. (Withdrawn) A method of screening for inhibitors of functions mediated by polypeptide GalNAc-transferase lectin domains which comprises using a polypeptide GalNAc-transferase or a fragment thereof retaining functional lectin binding in a binding assay where it interacts with a GalNAc or Gal β 1-3GalNAc O-glycopeptide ligand or a molecular mimic hereof, while the binding capacity of the catalytic domain is inactivated by the presence of EDTA or the

absence of UDP or UDP-GalNAc or Mn^{++} or other divalent metal ion, and measuring the binding inhibition to identify and evaluate efficiency of a potential inhibitor.

15. (Withdrawn) A compound that binds to the lectin domain of a member of the mammalian family of polypeptide GalNAc-transferases and inhibits the binding of a carbohydrate to said domain, wherein said compound does not serve as a substrate for core 1 β 1,3-galactosyltransferase activity or other glycosyltransferases acting in mucin O-glycosylation.

16. (Withdrawn) The compound of claim 15 wherein said said family of polypeptide GalNAc-transferases is human.

17. (Withdrawn) An inhibitor of polypeptide GalNAc-transferase lectin-mediated functions that selectively binds to the lectin domain of said transferase and does not serve as an acceptor substrate for core 1 β 1,3-galactosyltransferase or other glycosyltransferases functioning in O-glycosylation.

18. (Withdrawn) An inhibitor according to claim 17, which is GalNAc β 1-R.

19. (Withdrawn) An inhibitor according to claim 18 wherein R represents an aglycone.

20. (Withdrawn) An inhibitor according to claim 18 wherein R represents an aryl group.

21. (Withdrawn) An inhibitor according to claim 18 wherein R is selected from the group consisting of benzyl, phenyl, p-nitrophenyl, umbelliferyl, and naphthalenemethanol.

22. (Withdrawn) A method of inhibiting mucin secretion in a subject comprising administering an effective amount of a compound that binds to one or more lectin domains of members of a mammalian family of polypeptide GalNAc-transferases and inhibit binding of such domains to carbohydrates.

23. (Withdrawn) A method of inhibiting hypersecretion and accumulation of mucin in the lungs of a mammal suffering from a chronic obstructive respiratory pulmonary disease comprising administering to said mammal an effective amount of at least one agent that inhibits the binding of polypeptide GalNAc-transferase lectin domains to GalNAc-glycopeptides, wherein said agent is selected from the group consisting of GalNAc β 1-benzyl, a carbohydrate portion of GalNAc β 1-benzyl, a glycoconjugate that includes a carbohydrate portion of GalNAc β 1-benzyl or a derivative of either that inhibits the binding of GalNAc-glycopeptides to a GalNAc-transferase lectin domain.

24. (Withdrawn) The method of claim 23 wherein the agent is a glycoconjugate that includes a carbohydrate portion of GalNAc β 1-benzyl.

25. (Withdrawn) The method of claim 23 wherein said mammal is a human.

26. (Withdrawn) A method of inhibiting the secretion of mucin in a patient comprising administering to the patient a therapeutically effective amount of an agent selected from the group consisting of GalNAc β 1-benzyl, a carbohydrate portion of GalNAc β 1-benzyl, a glycoconjugate that includes a carbohydrate portion of GalNAc β 1-benzyl or a derivative of either that inhibits the binding of GalNAc-glycopeptides to a GalNAc-transferase lectin domain.

27. (Withdrawn) The method of claim 26, which selectively inhibits one or more members of the GalNAc-transferase family without inhibiting other glycosyltransferases selected

from the group consisting of core 1 β 1,3-galactosyltransferases, α 2,6-sialyltransferases, and glycosyltransferases functioning in the O-glycosylation pathway.

28. (Withdrawn) The method of claim 26 wherein the patient has a disease selected from the group consisting of chronic obstructive pulmonary diseases, asthma, and cystic fibrosis.

29. (Withdrawn) A method of modulating the function of one or more lectin domains of a polypeptide GalNAc-transferase comprising administering an effective amount of GalNAc β 1-R which is effective in modulating functions mediated by said lectin domains.

30. (Withdrawn) The method of claim 29 wherein R represents an aglycone.

31. (Withdrawn) The method of claim 29 wherein R represents an aryl group.

32. (Withdrawn) The method of claim 30 wherein R is selected from the group consisting of benzyl, phenyl, p-nitrophenyl, umbelliferyl, and naphthalenemethanol.

33. (Withdrawn) A method of screening one or more test substances for the ability to inhibit or modulate intracellular transport and/or cell surface expression of mucins, O-glycosylated glycoproteins, glycoproteins and proteins in a cell-based assay, which comprises:

- (i) contacting a cell that expresses mucins, O-glycosylated glycoproteins, glycoproteins and proteins, with one or more test substances under assay conditions suitable for the detection of inhibition or modulation of said expression; and

- (ii) measuring whether intracellular transport and cell surface expression of said mucins, O-glycosylated glycoproteins, glycoproteins and proteins are thereby inhibited or modulated by one or more of the substances.

34. (Withdrawn) A method of screening one or more test substances for the ability to inhibit or modulate secretions of mucins, O-glycosylated glycoproteins, glycoproteins and proteins in a cell-based assay, which comprises:

- (i) contacting a cell that secretes mucins, O-glycosylated glycoproteins, glycoproteins with one or more test substances under assay conditions suitable for the detection of inhibition or modulation of said secretion; and
- (ii) measuring whether secretion of said mucins, O-glycosylated glycoproteins, glycoproteins and proteins are thereby inhibited or modulated by one or more of the substances.

35. (Withdrawn) The method of claim 22, wherein the compound is GalNAc β 1-benzyl.

36. (Withdrawn) The method of claim 23, wherein the compound is GalNAc β 1-benzyl.

37. (Withdrawn) The method of claim 23, wherein the compound is GalNAc β 1-benzyl.

38. (Withdrawn) The method of claim 34, wherein step (ii) further comprises measuring whether the intracellular accumulation of said mucins, O-glycosylated glycoproteins and proteins is inhibited or modulated.

39. (Withdrawn) A method of inhibiting mucin secretion in a cell comprising delivering to a cell an effective amount of a compound that binds to one or more lectin domains of members of a mammalian family of polypeptide GalNAc-transferases and inhibit binding of such domains to carbohydrates.

40. (Withdrawn) The method of claim 39, wherein the compound is GalNAc β 1-benzyl.